DETAILED ACTION

Claims Under Examination

Claims 44-50 and 52-56 are under examination. Claims 1-43 and 51 have been canceled.

Priority

This application has been granted the benefit of priority to US Provisional Application 09/031,271, filed 2/27/1998. Applicant's claim for the benefit of priority to US Patent Application 08/810,983 filed Feb. 27, 1997 (now US Patent No. 5,989,835) under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is denied. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e). The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See Transco Products, Inc. v. Performance Contracting, Inc., 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 08/810,983, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Namely, the provisional application does not provide support for a machine readable storage medium comprising a program for causing a cell screening system to execute procedures for detecting a translocation between a first and second cellular compartment, as in claim 44, or for performing specific steps at multiple time points, as in claim 56. Priority is therefore only granted benefit of priority to US Provisional Application 09/031,271, filed 2/27/1998.

Withdrawn Rejections

The rejection of claims 44-50 and 52-56 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicant's amendment of claim 44, filed 02/06/2008, which provide antecedent basis for said results.

The rejection of claims 44-49, 53, and 56 under 35 U.S.C. 102 (b) as being anticipated by Kamentsky et al. (US 5,427,910; Issued Jun. 27, 1995) is withdrawn in view of applicant's amendments filed 02/06/2008, which requires a first and second cellular compartment be different, and translocation between a first and second cellular compartment, and further in view of applicant's arguments filed 02/06/2008, that Kamentsky does not teach translocation between a first and second cellular compartment.

The rejection of claims 44-50 and 52-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taylor (WO/1997/045730; Published Dec. 4, 1997), in view of Bastiaens et al. (Proc. Natl. Acad. Sci. USA, August 1996, Vol. 93, pp. 8407-8412) and the legal decision of *In re Venner* [262 F.2d91, 95, 120 USPQ 193, 194 (CCPA 1958)],) is withdrawn in view of applicant's amendments filed 02/06/2008, which requires a first and second cellular compartment be different, and translocation between a first and second cellular compartment, and further in view of applicant's arguments filed 02/06/2008, that Taylor does not teach translocation between a first and second cellular compartment.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 44-50 and 52-56 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter. Claims 44-50 and 52-56 are drawn to a machine readable storage medium comprising a program for carrying out a process. The claims must be limited only to statutory embodiments. In the instant case, the claimed machine readable storage medium is not embodied on a computer and does not comprise any limitations such that it is interpreted as a physical product. Additionally, the specification does not provide a limiting definition for machine readable storage medium. Therefore the claimed machine readable storage medium does not recite a tangible result in a form that is useful to the user of the process because the claims encompasses non-statutory embodiments of machine readable storage medium (e.g. carrier waves) which are not a tangible medium. For these reasons, the instant claims are not statutory.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C.102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 44-50 and 52-56 are rejected under 35 U.S.C. 102 (e) as being anticipated by Dunlay et al. (US 5,989,835; Issued Nov. 23, 1999; Filed Feb. 27, 1997). This rejection is newly applied.

Dunlay teaches an optical system and automated method (i.e. program) for determining the distribution or activity of fluorescently labeled reporter molecules in cells for screening compounds. In particular, Dunlay teaches software (i.e. computer readable medium) for defining cellular compartment masks in first and second cellular compartments [Col. 7 and Fig. 8], determining intensities and measuring ratios of intensities and difference of intensities [Col. 7, lines 30-45, and Fig. 10], and measuring cell fluorescent molecules and translocation from the cytoplasm to the nucleus [Col. 7, lines 45-60, Ref. Claims 1-7, and Fig. 8]. Dunlay also teaches cellular components of interest that are proteins [Example 2, Col. 11]. The system comprises a computer for storing and displaying data, and generating reports, as in claims 45-49 [Fig. 1, 4, 5, and 6]. The procedures can be performed recursively [Fig. 7]. Therefore claims 44-50 and 52-56 are anticipated.

Response to Arguments

Applicant's arguments filed 02/06/2008, that Kamentsky et al. does not teach translocation between a first and second cellular compartment, wherein the first and second compartment are different have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However,

upon further consideration, a new ground of rejection is made in view of applicant's arguments and amendments filed 2/06/2008 which requires different first and second cellular compartments, and translocation between different first and second cellular compartments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 44-50 and 52-56 are rejected under 35 U.S.C. 103(a) as being made obvious by Carey et al. (The Journal of Cell Biology, 1996, Vol. 133, No. 5, p.985-996; IDS Filed 08/18/2006), in view of Dow et al. (Cytometry, 1996, Vol. 25, p.71-81; IDS Filed 06/26/2007), and in view of Bastiaens et al. (Proc. Natl. Acad. Sci. USA, August 1996, Vol. 93, pp. 8407-8412). This rejection is newly applied.

Carey teaches a method for determining the translocation of micro-injected proteins from the cytoplasm to the nucleus in response to a receptor antagonist [Abstract]. Carey uses two different

fluorescent probes [p.986, Col. 2, Microscopy]. Fluorescent microscopy mages were quantitated by summing pixel values separately within the nucleus and within the cytoplasmic compartments [p.989, Col. 1, last ¶ and Col. 2]. Nuclear/cytoplasmic ratios are calculated using software [p.986, Col. 2, Microscopy]. Real-time fluorescent images of the cells are obtained to determine nuclear-cytosolic translocation of proteins [p.987, Results, and Fig. 1]. Carey also shows "nuclear/cytosolic" ratios to determine the translocation of different proteins over time [p.991]. Carey also shows qualitative measurements made by "eye" to assess nuclear-cytosolic redistribution [p.987, Col. 1].

Carey does not specifically teach defining first and second cellular compartment "masks", as in claim 44. Carey also does not specifically teach determining an ratio of the intensity signals from a first and second cellular compartment", as in claims 44, 50, and 52.

Dow teaches an automated system that identifies both nuclear and cytoplasmic boundaries of cell [Abstract]. In particular, Dow provides computer algorithms for defining cellular compartment masks in a plurality of cells using image segmentation [p.72, Col. 1, p.73, Image Analysis, and Fig. 1]. Dow uses fluorescent nuclear DNA probes and antibodies that are optically distinguishable [p.72, Col. 1, p.78, Fig. 3 and Fig. 6]. Dow detects intensity measurements of labeled probes to determine nuclear boundaries using nuclear probes [p.72, Col. 1, ¶4, and p.76, Cell Classification] as well as cellular boundaries using surface bound antibodies [p.77, Feature Extraction]. Dow also suggests their system can be modified to utilize improved probes that define tissue compartments and cellular structure [p.80, Col. 1].

Bastiaens teaches a computer-based system for observing the translocation of fluorescent labeled proteins and determining their molecular state in different cellular compartments [p.8407, Col. 1 and Col. 2, ¶1]. In particular, confocal microscopy images are obtained of the optically distinct probes to assess the sub-cellular distribution of the PKC protein [p.8408, Col. 1, Imaging Techniques, and Col. 2, Results]. Efficiency is determined by obtaining the ratio of fluorescent probes before and after [p.8409, Col. 2, ¶2]. The localization of two different fluorescent labeled proteins in cells is displayed such that differences

between the two labels are presented as color-coded fluorescent intensity profiles as a measure of translocation of microinjected proteins from the cytoplasm into the cell nucleus [Fig. 3, 5, and 6, and p.8409, Col. 2]. Labeled proteins can be followed at multiple time intervals [p.8408, Col. 1, ¶3 and 8410, Col. 2].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the method of Carey to use the automated segmentation technique of Dow, since both Carey and Dow are directed to the field of fluorescent microscopy. One of ordinary skill in the art would have been motivated to combine the above teachings in order to improve cellular analysis with an automated, fast, and consistent system for segmenting cells, as suggested by Dow [p.79, Discussion]. It would further have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the methods of Carey and Dow using the computer-based system of Bastiaens in order to automatically determine cellular translocation of proteins using multiple probes, resulting in the practice of the instantly claimed invention with predictable results.

Claims 44-50, 52, 53, and 56 are rejected under 35 U.S.C. 103(a) as being made obvious by Mason et al. (Fluorescent and Luminescent Probes for Biological Activity, 1993, Chapter 12, p.161-195), in view of Wright et al. (Journal of Experimental Botany, March 1996, Vol. 47, No. 296, pp. 439-445). This rejection is newly applied.

Mason et al. teach a computer system for fluorescent ratio imaging of cells [p.174, Section 12.13]. The system includes software and hardware for storage, analysis, and display of all data, as in claims 44-49. In particular, the system provides a means for spatial digitization of cells (i.e. masking) [See Fig. 12.15 and Plate 29.1 for example], wherein pixel intensity profiling [See Fig. 12.16, Plate 29.1, and 29.2] and ratio analysis [Plate 13.2] are both used to compare spatial and temporal differences in the

distribution (i.e. translocation) of fluorescent probes at a plurality of locations between different cellular compartments which include the cytoplasm, cell wall, and nucleus, as in claims 44, 50, 52, 53, and 56.

Mason et al. do not specifically teach the translocation between the nucleus and cytoplasm and the cytoplasm and cell member based on differences between two different probe signals, as in claim 50 and 52. However, Mason et al. clearly teach the use of different types of probes for measuring cellular distribution [See Plate 10.1 additionally]. Therefore, it would be well within the ordinary skill of one in the art to use the differences in optical density measurements of obtained from different probes accumulated in the cell nuclei or cytoplasm [Fig. 9] as a measure of translocation of material between the cell nucleus or cytoplasm, as in claims 50 and 52.

Wright et al. teach the use of confocal microscopy techniques for determining the intercellular distribution (i.e. translocation) of multiple fluorescent probes in plant cells [Abstract], and results wherein the translocation of fluorescent markers was observed in the cytoplasm and nuclei of adjacent cells [p.441, Results] and [Fig. 2A, 2B], which also includes translocation across the cell membrane. Therefore Wright et al. teaches the limitations of claims 50, 52, and 53.

Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to use the system of Mason et al. for analyzing the intercellular fluorescent markers, taught by Wright et al., as Mason et al. clearly teach the use of confocal microscopy for analysis of cellular specimens [Section 12.9], where the motivation would be have been to improve the determination of cell-to-cell interactions and intercellular pathways in plants [Wright et al., p.444, Col. 1].

Response to Arguments

Applicant's arguments filed 02/06/2008 directed to Mason et al. have been fully considered but

are not persuasive for the following reasons.

In response to applicant's arguments that Mason et al. does not teach, suggest or make obvious measuring translocation of a cellular component of interest between first and second cellular compartments of interest, Mason shows the distribution of fluorescent probes throughout the cell in space and time, which generally shows translocation [See Fig. 12.16, Plates 10.1, 13.2, 29.1, and 29.2]. However, Mason was not relied upon as a teaching for translocation of a cellular component between the nucleus and cytoplasm and the cytoplasm and cell member based on differences between two different probe signals, as set forth in the Office action mailed 9/20/2007 [p.7, ¶2].

In response to applicant's arguments that Mason et al. does not teach defining a mask of a first cellular compartment and a second cellular compartment wherein the first and second cellular compartments are different, Mason shows fluorescent imaging wherein first and second cellular compartments are different [Plates 10.1 and 12.8].

In response to applicant's arguments that Mason et al. does not teach determining the ratio or difference of the intensity of the luminescent signals in the first and second cellular compartments masks (i.e. in different cellular compartments), Mason teaches pixel intensity profiling [See Fig. 12.16, Plate 29.1, and 29.2] and ratio analysis [Plate 13.2], which reads on determining the ratio of different probes.

In response to applicant's arguments that the combination of Mason and Wright does teach translocation between a first and second compartment as claimed, Wright teaches confocal microscopy techniques for determining the intercellular distribution (i.e. translocation) of multiple fluorescent probes and shows translocation of fluorescent markers between the cytoplasm and nuclei of adjacent cells [p.441, Results, and Fig. 2A, 2B], which reads on translocation between a first and second cellular compartment. It is noted that the instant claim 44 recites translocation between compartments on or within individual cells, which reads on intra-cellular and inter-cellular translocation. This rejection is maintained.

Applicant's arguments filed 02/06/2008 that the Taylor reference is not a proper prior art reference according to the MPEP are not persuasive, because applicant's claim for the benefit of priority to US Patent Application 08/810,983 filed Feb. 27, 1997 (now US Patent No. 5,989,835) under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is denied because US Patent Application 08/810,983 fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Namely, the provisional application does not provide support for a machine readable storage medium comprising a program for causing a cell screening system to execute procedures for detecting a translocation between a first and second cellular compartment, as in claim 44, or for performing specific steps at multiple time points, as in claim 56. Accordingly, application is granted the benefit of priority to US Provisional Application 09/031,271, filed 2/27/1998. Since Taylor was published Dec. 4, 1997 (corrected from the previous Office action which erroneously set forth a publication data of Dec. 12, 1997), Taylor remains proper prior art under 35 U.S.C. 102 (a).

Applicant's arguments filed 02/06/2008, that Taylor does not teach translocation between a first and second cellular compartment, wherein the first and second compartment are different have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of applicant's amendments filed 2/06/2008 which requires different first and second cellular compartments, and translocation between different first and second cellular compartments.

Conclusion

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action

is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached at 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Pablo S. Whaley/

Patent Examiner

Art Unit 1631

/John S. Brusca/
Primary Examiner, Art Unit 1631